AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [0008] with the following rewritten paragraph:

— **[0008]** In the last few years, oligopeptides have been reported as being effective in modulating immune system activity and extending the lifetime of allogeneic transplants. These oligopeptides are based on the human leukocyte antigen-B (HLA-B) α1-domain and have a conserved amino acid sequence Arg-X-X-X-Arg-X-X-X-X-Tyr (SEQ ID NO:1), with the various amino acids designated as X varying within a relatively few amino acids to retain activity (e.g., see WO 95/13288). The mechanism by which these oligopeptides effectuate their activity is not understood, particularly as to how they cooperate with subtherapeutic doses of cyclosporin to extend the lifetime of allogeneic transplants. —

Please replace paragraph [0009] with the following rewritten paragraph:

— **[0009]** Also reported (Manolios, NOVEL PEPTIDE, PCT application, filed based on Australian application Nos. PN 0589 and PN 0590, January 16, 1995) as having an effect on T cell mediated inflammation are oligopeptides of the formula:

A-B-C-D-E

wherein: A is absent or is 1 or 2 hydrophobic residues; B is a positively charged amino acid; C is a peptide consisting of from 3 to 5 hydrophobic amino acids; D is a positively charged amino acid; and E is absent or is up to 8 hydrophobic amino acids. The peptides that were synthesized are: Gly-Leu-Arg-Ile-Leu-Leu-Leu-Lys-Val (SEQ ID NO:2); Met-Gly-Leu-Arg-Ile-Leu-Leu-Leu (SEQ ID NO:3); Leu-Gly-Ile-Leu-Leu-Leu-Gly-Val (SEQ ID NO:4); Leu-Asp-Ile-Leu-Leu-Leu-Gly-Val (SEQ ID NO:5); Leu-Arg-Ile-Leu-Leu-Leu-Ile-Leu-Val (SEQ ID NO:6); and Leu-Arg-Leu-Leu-Leu-Lys-Val (SEQ ID NO:7). The sequences are predicated on the sequence of a transmembrane sequence of TCR-α. There is no support in this application that the peptides have a beneficial effect on extending transplantation lifetimes. —

Please replace paragraph [0011] with the following rewritten paragraph:

— **[0011]** Cytomodulating peptides are provided which are capable of (1) modulating the activity of various immune system cells, particularly lymphocytic cells, more particularly CTLs, (2) inhibiting the production of inflammatory cytokines by cells capable of producing such cytokines, thereby being effective in the treatment of conditions associated with adverse inflammatory reactions, (3) modulating

the activity of heme-containing enzymes and/or (4) delaying the onset of insulin-dependent diabetes mellitus (IDDM) in a host susceptible of having IDDM, where the peptides are based upon a design in accordance with a computer program. Exemplary of the compounds are oligopeptides comprising the sequence B-X-X-X-B-X-X-X-J-Tyr (SEQ ID NO:8), where B is a basic amino acid, J is Gly, B, or an aliphatic hydrophobic amino acid of from 5-6 carbon atoms and X is any amino acid other than an aliphatic polar amino acid, where at least three Xs are the same aliphatic non-polar amino acid, dimers thereof and D-stereoisomers thereof, and wherein the amino acid sequence may be part of a ring. The peptides find use for inhibiting the activation of immune system lymphocytes, particularly cytotoxic lymphocytes, either by themselves or in conjunction with other immunosuppressant agents, particularly in extending the lifetime of transplants. The peptides described herein also find use for inhibiting the production of inflammatory cytokines (e.g., interferon-γ, IL-1, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, IL-13, IL-16, MIP1α, etc.), thereby being useful for inhibiting inflammatory responses associated with various disorders such as rheumatoid arthritis, septic shock, Crohn's disease, colitis, allergic reactions, autoimmune diseases, and the like, for inhibiting the activity of heme-based enzymes such as heme oxygenase, nitric oxide synthase, etc., and delaying the onset of IDDM in a patient at risk for developing IDDM, both *in vitro* and *in vivo*. Administration of the peptides may be *ex vivo* of an organ to be transplanted or *in vivo* by any convenient means, including by direct application or administration of the peptide or nucleic acid encoding the desired peptide, in sufficient amount to substantially inhibit lymphocytic activation, inhibit the production of inflammatory cytokines and the associated inflammatory process, inhibit heme-based enzyme activity, an activity that has been previously associated with inflammatory responses and/or delaying the onset of IDDM. —

Please replace paragraph [0017] with the following rewritten paragraph:

— **[0017]** New isolated peptide compounds were devised comprising the sequence B-X-X-X-B-X-X-X-J-Tyr (SEQ ID NO:9), where B is a basic amino acid, namely Lys or Arg, particularly Arg at at least one position, preferably at both positions, J is Gly, B or an aliphatic hydrophobic amino acid of from 5 to 6 carbon atoms, particularly Gly or B, and X is any amino acid other than an aliphatic charged amino acid, preferably any amino acid other than a polar amino acid, where at least three Xs are the same aliphatic non-polar amino acid, preferably at least 4 are the same aliphatic non-polar amino acid, and more preferably at least all but one are the same aliphatic non-polar amino acid, oligomers, particularly, dimers thereof and D-stereoisomers thereof, and wherein the amino acid sequence may be part of a ring.
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Please replace paragraph [0022] with the following rewritten paragraph:

— **[0022]** Of the six amino acids indicated by X in the B-X-X-X-B-X-X-X-J-Tyr (SEQ ID NO: 10) peptide sequence, preferably at least 3 are aliphatic amino acids of from 5 to 6 carbon atoms, more preferably at least 4 are aliphatic amino acids of from 5 to 6 carbon atoms, more particularly 6 carbon atoms. The other amino acids may be other uncharged aliphatic amino acids, particularly non-polar aliphatic amino acids or aromatic amino acids. —

Please replace paragraph [0024] with the following rewritten paragraph:

— **[0024]** Compositions of particular interest will have the following formula:

Arg-U-X-X-Arg-X-X-X-J-Tyr (SEQ ID NO:11)

wherein all of the symbols have been defined previously except U and U is an uncharged aliphatic amino acid or aromatic amino acid, particularly a non-polar aliphatic amino acid or aromatic amino acid. —

Please replace paragraph [0068] with the following rewritten paragraph:

— **[0068]** Starting from the consensus sequence Arg-X-X-X-Arg-X-X-X-X-Tyr (SEQ ID NO:1) where X is an amino acid which is as defined in the earlier analogous formula, the physicochemical and topological parameters previously described were computed and whether these parameters were within the constraints defined by the initial training set. For example, starting from X=Leu, nLeu, Trp, Tyr, Gly or Val, a library of 279,936 molecules was generated and only 26 of them satisfied the required constraints. —

Please replace paragraph [0073] with the following rewritten paragraph:

— **[0073]** Applied to HLA-B2702.75-84 peptide (amino acid sequence Arg-Glu-Asn-Leu-Arg-Ile-Ala-Leu-Arg-Tyr) (SEQ ID NO:12) and on various active and inactive derivative peptides thereof, molecular dynamics simulations were performed using AMBER 4.1. The simulation of one nanosecond of dynamics generate a set of 10^3 conformations (one conformation per picosecond). For each conformation the 3D autocorrelation vector was calculated using TSAR with a distance increment of 1 Å and the entire set of conformations was stored as 3D autocorrelation vectors versus time matrix (10^3xn).
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Please replace paragraph [0077] with the following rewritten paragraph:

— **[0077]** Figure 1 shows the two-dimensional conformational space and related conformations of peptide bc1-nL, wherein the bc1-nL peptide has the amino acid sequence Arg-nL-nL-nL-Arg-nL-nL-nL-Gly-Tyr (SEQ ID NO:13) and wherein "nL" is norleucine (see below). The structures drawn were obtained by applying cluster analysis method on the whole trajectory of peptide bc1-Nl. —

Please replace paragraph [0079] with the following rewritten paragraph:

— **[0079]** The trajectory of the D2 (amino acid sequence Arg-Val-Asn-Leu-Arg-Ile-Ala-Leu-Arg-Tyr) (SEQ ID NO:14) peptide has been described by the 3-D autocorrelation method and the data analyzed by principal component analysis. This provided a principal plan defined by the 2 first principal components which contain all the conformations visited during the trajectory. The D2 peptide trajectory was used as a trajectory reference and all the trajectories calculated were projected into its principal plan. (Figure 2) —

Please replace paragraph [0081] with the following rewritten paragraph:

— **[0081]** The following peptides were prepared as compositions.

bc #										SEQ ID NO
1	Arg	Leu	Leu	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:15
2	Arg	Val	Leu	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:16
3	Arg	Ile	Leu	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:17
4	Arg	Leu	Val	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:18
5	Arg	Leu	Ile	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:19
6	Arg	Leu	Leu	Val	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:20
7	Arg	Leu	Leu	Ile	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:21
8	Arg	Leu	Leu	Leu	Arg	Val	Leu	Leu	Gly	Tyr	SEQ ID NO:22
9	Arg	Leu	Leu	Leu	Arg	Ile	Leu	Leu	Gly	Tyr	SEQ ID NO:23

10	Arg	Leu	Leu	Leu	Arg	Leu	Val	Leu	Gly	Tyr	SEQ ID NO:24
11	Arg	Leu	Leu	Leu	Arg	Leu	Ile	Leu	Gly	Tyr	SEQ ID NO:25
12	Arg	Leu	Leu	Leu	Arg	Leu	Leu	Val	Gly	Tyr	SEQ ID NO:26
13	Arg	Leu	Leu	Leu	Arg	Leu	Leu	Ile	Gly	Tyr	SEQ ID NO:27
14	Arg	Trp	Leu	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:28
15	Arg	Leu	Trp	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:29
16	Arg	Leu	Leu	Trp	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:30
17	Arg	Leu	Leu	Leu	Arg	Trp	Leu	Leu	Gly	Tyr	SEQ ID NO:31
18	Arg	Leu	Leu	Leu	Arg	Leu	Trp	Leu	Gly	Tyr	SEQ ID NO:32
19	Arg	Leu	Leu	Leu	Arg	Leu	Leu	Trp	Gly	Tyr	SEQ ID NO:33
20	Arg	Tyr	Leu	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:34
21	Arg	Leu	Tyr	Leu	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:35
22	Arg	Leu	Leu	Tyr	Arg	Leu	Leu	Leu	Gly	Tyr	SEQ ID NO:36
23	Arg	Leu	Leu	Leu	Arg	Tyr	Leu	Leu	Gly	Tyr	SEQ ID NO:37
24	Arg	Leu	Leu	Leu	Arg	Leu	Tyr	Leu	Gly	Tyr	SEQ ID NO:38
25	Arg	Leu	Leu	Leu	Arg	Leu	Leu	Tyr	Gly	Tyr	SEQ ID NO:39
1nL	Arg	nL	nL	nL	Arg	nL	nL	nL	Gly	Tyr	SEQ ID NO:13

nL = norleucine —

Please replace paragraph [0086] with the following rewritten paragraph:

— **[0086]** The results obtained from these studies demonstrated that while a PBS/DMSO solution lacking peptide and a control peptide 2705 (amino acid sequence Arg-Glu-Asp-Leu-Arg-Thr-Leu-Leu-Arg-Tyr) (SEQ ID NO:40) had no effect on T-cell proliferation, bc peptides inhibited T-cell proliferation between 35% and 75%. These data, therefore, demonstrate that bc peptides exhibit remarkable abilities to inhibit T-cell proliferation. —

Please replace paragraph [0090] with the following rewritten paragraph:

— **[0090]** The results of these analyses demonstrated that control peptide 2702.75-84 (amino acid sequence Arg-Glu-Asn-Leu-Arg-Ile-Ala-Leu-Arg-Tyr) (SEQ ID NO:41) administered at 80mg/kg/day (days 0-9) prolonged heart allograft survival to 10.7 ± 2.6 days, compared to 8 ± 1.4 days in control animals treated with PBS/DMSO ($p<0.01$). Administration of control peptide 2702.75-84 at 40mg/kg/day had no observable effect on transplant survival over the control treatment. In contrast, however, administration of bc peptides as low as 1mg/kg/day resulted in a significant prolongation of heart allograft survival with 50% of the grafts surviving for more than 28 days. These results demonstrate, therefore, that bc peptides have immunosuppressive activities sufficient to enhance survival of transplants in mammals. —

Please replace paragraph [0097] with the following rewritten paragraph:

— **[0097]** The results from these experiments demonstrated that while the control peptide D2RP (amino acid sequence Arg-Val-Asn-Leu-Pro-Ile-Ala-Leu-Arg-Tyr) (SEQ ID NO:42) showed no ability to inhibit the production of TNF-α by RAW264.7 macrophage cells, bc peptides inhibited the production of TNF-α in a dose dependent manner. Thus, bc peptides will find use in inhibiting the production of inflammatory cytokines, thereby having beneficial utility in the treatment of inflammation and inflammation-associated disorders. —

Please insert the enclosed 14-page text entitled "SEQUENCE LISTING" immediately preceding the claims.